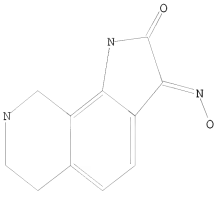

Structure attributes must be viewed using STN Express query preparation.

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=> s l1
SAMPLE SEARCH INITIATED 12:31:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       35 TO ITERATE

100.0% PROCESSED       35 ITERATIONS                              11 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          346 TO     1054
PROJECTED ANSWERS:              22 TO      418

L2           11 SEA SSS SAM L1

=> s l1 full
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100.0% PROCESSED      620 ITERATIONS                             213 ANSWERS
SEARCH TIME: 00.00.01

L3          213 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                  178.36     178.57

FILE 'CAPLUS' ENTERED AT 12:31:28 ON 27 AUG 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 27 Aug 2008 VOL 149 ISS 9
FILE LAST UPDATED: 26 Aug 2008 (20080826/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/legal/infopolicy.html

=> s l3
L4 37 L3

=> s l4 and enantiomers
29723 ENANTIOMERS
L5 3 L4 AND ENANTIOMERS

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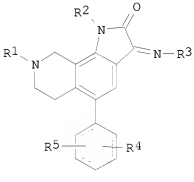
L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
GI



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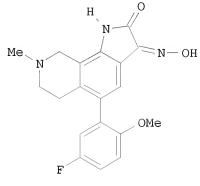

II

AB Pyrrolo-isoquinoline compds. according to formula I is disclosed. Compds. of formula I wherein dashed lines are single or double bonds; R1 is H, alkyl, alkoxy-alkyl, hydroxyalkyl, alkoxycarbonyl-alkyl, etc.; R2 is H, OH, alkyl, alkenyl, (CH2)1-4CO2H, CO-C1-4 alkyl, and SO2-C1-4 alkyl; R3 is H, OH, alkyl, acyl, benzyl, CO2H, CONMe2, OPh, OCF3, alkoxy, etc.; R4 and

R5 are independently halo, CF3, NO2, NH2, CN, OH, alkoxy, PhO, Ph, SO2NH2 and derivs.; and their pharmaceutically acceptable salts, enantiomers, stereoisomers, rotamers, tautomers, diastereoisomers, and racemates thereof, are claimed. These compds. and their pharmaceutical acceptable salts are used for modulating gated ion channels in order to treat pain, inflammatory disorders, neurol. disorders, or diseases associated with the genitourinary or gastrointestinal systems. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their ASIC antagonistic activity. From the assay, it was determined that compound II exhibited IC50 values of 0.10-0.20 μM.

AN 2007:590735 CAPLUS
DN 147:30964
TI Pyrroloisoquinolines and their preparation, compositions and methods for modulating gated ion channels
IN Vohra, Rahul; Demnitz, Joachim; Ahring, Philip K.; Gan, Zhonghong; Gill, Nachhattarpal
PA Painceptor Pharma Corporation, Can.
SO PCT Int. Appl., 118pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007059608	A1	20070531	WO 2006-CA1897	20061122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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			US 2005-739600P	P 20051123
			WO 2006-CA1897	W 20061122
US 20070191418	A1	20070816	US 2006-603946	20061122
			US 2005-739600P	P 20051123
EP 1957486	A1	20080820	EP 2006-804755	20061122
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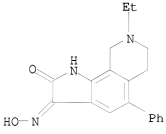
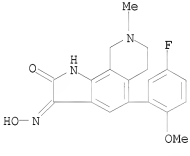
			US 2005-739600P	P 20051123
			WO 2006-CA1897	W 20061122
KR 2008070749	A	20080730	KR 2008-714653	20080617
			US 2005-739600P	P 20051123
			WO 2006-CA1897	W 20061122
IN 2008DN05376	A	20080808	IN 2008-DN5376	20080620
			US 2005-739600P	P 20051123
			WO 2006-CA1897	W 20061122

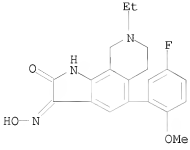
OS MARPAT 147:30964
IT 309711-59-9P 938170-27-5P 938170-28-6P
938170-29-7P 938170-30-0P 938170-31-1P
938170-32-2P 938170-33-3P 938170-34-4P
938170-35-5P 938170-36-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrroloisoquinoline compds. as voltage-gated ion channel modulators useful in treatment of diseases)
RN 309711-59-9 CAPLUS
CN 1H-Pyrrolo[3,2-h]isoquinoline-2,3-dione, 8-ethyl-6,7,8,9-tetrahydro-5-phenyl-, 3-oxime (CA INDEX NAME)



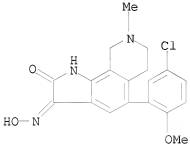
RN 938170-27-5 CAPLUS
CN 1H-Pyrrolo[3,2-h]isoquinoline-2,3-dione, 5-(5-fluoro-2-methoxyphenyl)-6,7,8,9-tetrahydro-8-methyl-, 3-oxime (CA INDEX NAME)



RN 938170-28-6 CAPLUS
CN 1H-Pyrrolo[3,2-h]isoquinoline-2,3-dione, 8-ethyl-5-(5-fluoro-2-methoxyphenyl)-6,7,8,9-tetrahydro-, 3-oxime (CA INDEX NAME)



RN 938170-29-7 CAPLUS
CN 1H-Pyrrolo[3,2-h]isoquinoline-2,3-dione, 5-(5-chloro-2-methoxyphenyl)-6,7,8,9-tetrahydro-8-methyl-, 3-oxime (CA INDEX NAME)



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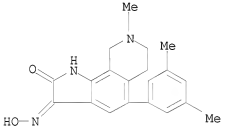

RN 938170-31-1 CAPLUS
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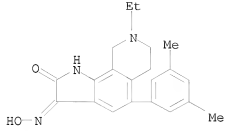

RN 938170-32-2 CAPLUS
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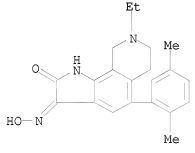
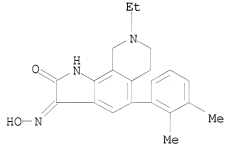
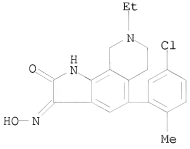


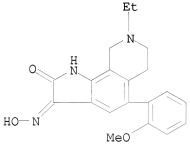
RN 938170-33-3 CAPLUS
CN 1H-Pyrrolo[3,2-h]isoquinoline-2,3-dione, 5-(2,3-dimethylphenyl)-8-ethyl-6,7,8,9-tetrahydro-, 3-oxime (CA INDEX NAME)



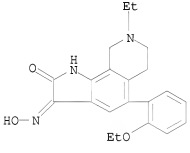
RN 938170-34-4 CAPLUS
CN 1H-Pyrrolo[3,2-h]isoquinoline-2,3-dione, 5-(5-chloro-2-methylphenyl)-8-ethyl-6,7,8,9-tetrahydro-, 3-oxime (CA INDEX NAME)



RN 938170-35-5 CAPLUS
CN 1H-Pyrrolo[3,2-h]isoquinoline-2,3-dione, 8-ethyl-6,7,8,9-tetrahydro-5-(2-methoxyphenyl)-, 3-oxime (CA INDEX NAME)

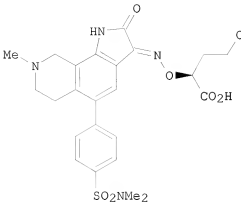


RN 938170-36-6 CAPLUS
CN 1H-Pyrrolo[3,2-h]isoquinoline-2,3-dione, 5-(2-ethoxyphenyl)-8-ethyl-6,7,8,9-tetrahydro-, 3-oxime (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
GI



I

AB The present invention is directed to a method of preparing enantiomers of indole-2,3-dione-3-oxime derivs., which method comprises the subsequent steps of (i) reacting an 8-amino-1,2,3,4-tetrahydroisoquinoline derivative with chloral hydrate and hydroxylamine hydrochloride to give an N-(1,2,3,4-tetrahydroisoquinolin-8-yl)-2-hydroxyiminoacetamide derivative; [ii] adding sulfuric acid to the N-(1,2,3,4-tetrahydroisoquinolin-8-yl)-2-hydroxyiminoacetamide derivative obtained in step (i); and (iii) reacting the 2,3-dioxo-2,3,6,7,8,9-hexahydro-1H-pyrrolo[3,2-h]isoquinoline derivative obtained in step [ii] with chiral [enantiopure (R) or (S)] α-N,N-diBoc-aminoxy-butyrolactone to obtain the desired chiral end product, i.e. enantiopure (R)- or (S)-2-(2-oxo-1,2,6,7,8,9-hexahydropyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy)-4-hydroxybutyric acid; followed by recovery of the desired end product. Thus, a suspension of 60% NaH (50 mg, 1.25 mmol) in dry DMF (4 mL) was added to a solution of 8-methyl-5-[4-(N,N-dimethylsulfamoyl)phenyl]-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime (isatin oxime derivative) (500 mg, 1.25 mmol) in dry DMF (8 mL) under N at 0°, stirred for 30 min at 0°, treated with a solution of (R)-α-tosyloxy-γ-butyrolactone (340 mg, 1.33 mmol) in dry DMF (2 mL), and stirred at room temperature overnight to give, after workup, (S)-2-[5-(4-dimethylsulfamoylphenyl)-8-methyl-2-oxo-1,2,6,7,8,9-hexahydropyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxybutyric acid (I).

AN 2004:182878 CAPLUS

DN 140:217629

TI A method of preparing enantiomers of indole-2,3-dione-3-oxime derivatives

IN Gouliaev, Alex Haahr; Brown, William Dalby; Waetjen, Frank

PA Neurosearch A/S, Den.

SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004018466	A2	20040304	WO 2003-DK539	20030813
	WO 2004018466	A3	20040325		

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EP 1532146	A2	20050525		EP 2003-792147		20030813
EP 1532146	B1	20060301				

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MX 2005PA02056	A	20050608		MX 2005-PA2056		20050221
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				WO 2003-DK539	W	20030813
US 20060178391	A1	20060810		US 2005-524441		20050810
				DK 2002-1237	A	20020822
				WO 2003-DK539	W	20030813

OS CASREACT 140:217629; MARPAT 140:217629

IT 666706-37-2P, 4-(3-Hydroxyimino-8-methyl-2-oxo-2,3,6,7,8,9-hexahydro-1H-pyrrolo[3,2-h]isoquinolin-5-yl)-N,N-dimethylbenzenesulfonamide sulfate 666706-40-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method of preparing enantiomers of indoledione oxime derivs.)

RN 666706-37-2 CAPLUS

CN Benzenesulfonamide, 4-[2,3,6,7,8,9-hexahydro-3-(hydroxyimino)-8-methyl-2-oxo-1H-pyrrolo[3,2-h]isoquinolin-5-yl]-N,N-dimethyl-, sulfate (1:1) (CA INDEX NAME)

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CRN 178431-82-8
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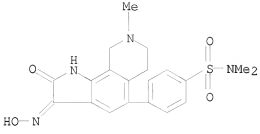
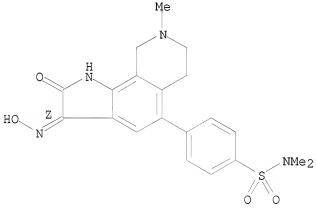


CM 2

CRN 7664-93-9
CMF H2 O4 S

RN 666706-40-7 CAPLUS
CN Benzenesulfonamide, 4-[(3Z)-2,3,6,7,8,9-hexahydro-3-(hydroxyimino)-8-methyl-2-oxo-1H-pyrrolo[3,2-h]isoquinolin-5-yl]-N,N-dimethyl- (CA INDEX NAME)

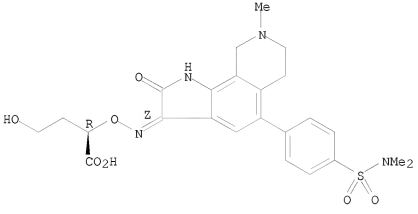
Double bond geometry as shown.



IT 666706-38-3P 666706-39-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(method of preparing enantiomers of indoledione oxime derivs.)
RN 666706-38-3 CAPLUS
CN Butanoic acid, 2-[[(Z)-[5-[4-[(dimethylamino)sulfonyl]phenyl]-1,2,6,7,8,9-

hexahydro-8-methyl-2-oxo-3H-pyrrolo[3,2-h]isoquinolin-3-ylidene]amino]oxy]-4-hydroxy-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 666706-39-4 CAPLUS
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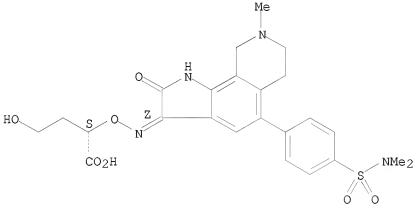
Absolute stereochemistry.
Double bond geometry as shown.

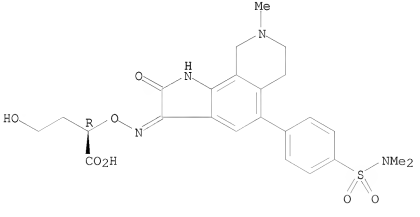


L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
AB The development of first generation AMPA antagonists as potential therapeutics for acute neurodegenerative conditions was hampered by insufficient water solubility, poor brain penetration and rapid kidney excretion of the compds. After more than ten years of research in academia and industry, novel compds. displaying far better properties entered clin. trials. In the present study, the in vitro and in vivo

pharmacol. properties of the novel potent and water soluble AMPA antagonist SPD 502 was evaluated together with its two enantiomers NS1219 and NS1220. In whole cell patch clamp studies on cultured mouse cortical neurons, SPD 502, NS1219 and NS1220 were shown to inhibit responses to AMPA with IC50 values of 210, 181 and 304 nM, resp. In HEK293 cells expressing homomeric GluR5 or GluR6 receptors, SPD 502 competitively inhibited kainate responses with IC50 values of 75 nM and 4500 nM, resp. Using in vivo electrophysiol. techniques, it was shown that SPD 502 inhibited climbing fiber evoked field excitatory postsynaptic potentials in rat cerebellar cortex after an i.v. dose of 5 mg/kg (.apprx.33% inhibition) and 10 mg/kg (.apprx.50% inhibition). In rat permanent medial cerebral artery occlusion (MCAO), SPD 502 (8 mg/kg bolus injection 3 h post-occlusion followed by a 4 mg/kg/h infusion for 24 h) resulted in a 21% reduction in ischemia-induced infarction.

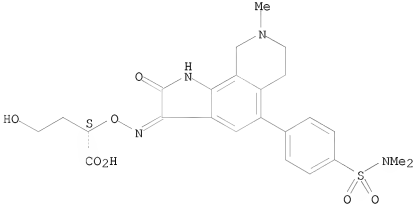
AN 2002:222659 CAPLUS
DN 137:242031
TI Optimization of isatin oximes as neuroprotective AMPA receptor antagonists: In vitro and in vivo evaluation of SPD 502
AU Varming, Thomas; Ahring, Philip K.; Sager, Thomas N.; Mathiesen, Claus; Johansen, Tina H.; Watjen, Frank; Drejer, Jorgen
CS NeuroSearch A/S, Ballerup, DK-2750, Den.
SO Biomedical and Health Research (2001), 45(Excitatory Amino Acids: Ten Years Later), 193-205
CODEN: BIHREN; ISSN: 0929-6743
PB IOS Press
DT Journal
LA English
IT 233603-81-1, NS 1219
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NS 1219; optimization of isatin oximes as neuroprotective AMPA receptor antagonists, with emphasis on in vitro and in vivo evaluation of SPD 502)
RN 233603-81-1 CAPLUS
CN Butanoic acid, 2-[[[5-[4-[(dimethylamino)sulfonyl]phenyl]-1,2,6,7,8,9-hexahydro-8-methyl-2-oxo-3H-pyrrolo[3,2-h]isoquinolin-3-ylidene]amino]oxy]-4-hydroxy-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

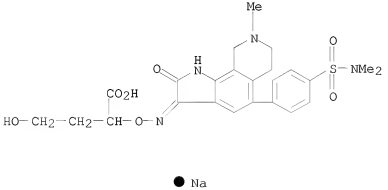


IT 233603-82-2, NS 1220
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NS 1220; optimization of isatin oximes as neuroprotective AMPA receptor antagonists, with emphasis on in vitro and in vivo evaluation of SPD 502)
RN 233603-82-2 CAPLUS
CN Butanoic acid, 2-[[[5-[4-[(dimethylamino)sulfonyl]phenyl]-1,2,6,7,8,9-hexahydro-8-methyl-2-oxo-3H-pyrrolo[3,2-h]isoquinolin-3-ylidene]amino]oxy]-4-hydroxy-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



IT 205645-02-9, SPD 502
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SPD 502; optimization of isatin oximes as neuroprotective AMPA receptor antagonists, with emphasis on in vitro and in vivo evaluation of SPD 502)
RN 205645-02-9 CAPLUS
CN Butanoic acid, 2-[[[5-[4-[(dimethylamino)sulfonyl]phenyl]-1,2,6,7,8,9-hexahydro-8-methyl-2-oxo-3H-pyrrolo[3,2-h]isoquinolin-3-ylidene]amino]oxy]-4-hydroxy-, sodium salt (1:1) (CA INDEX NAME)



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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